REMARKS

Claims 81 and 82 are currently pending. Claim 81 is allowed. Claim 80 is cancelled without prejudice to the prosecution of its subject matter in other patent applications. New claim 82 is supported by the specification and does not contain new matter.

1. Inventorship

It has recently come to the attention of Attorneys for Applicant that inventorship of the application needs to be corrected. Attorneys for Applicant are presently finalizing their inventorship investigation. The required documents will be submitted shortly.

2. The Claims Are Supported By The Specification

Claim 80 is rejected under 35 U.S.C. §112 as failing to comply with the written description requirement. In particular, the Examiner contends that the phrase "binds to an antibody directed toward the peptide fragment of SEQ ID NO:2 having the sequence Pro-Ser-Gln-Glu-Asn-Glu-Met-Phe-Ser-Ile-Arg-Asp (SEQ ID NO:5)" constitutes new matter, because, according to the Examiner, the antibody disclosed in the specification does not contemplate the nucleic acid sequences encompassed by claim 80.

Applicant respectfully disagrees. Paragraph 42, cited by the Examiner, which corresponds to paragraph 47 of the published version of the application (20030082140 A1) describes ways to detect an increase in MDA-7 protein. The specification defines "MDA-7 protein" as not being confined to a single sequence, but

rather a relatively narrow genus of functionally equivalent molecules. Paragraph 46 of the published application states:

> The scope of the invention embraces functional equivalents of the nucleic acid and protein which vary in insignificant ways from the native molecules; for example, it includes isolated nucleic acids which hybridize to the nucleic acid sequence set forth as SEQ ID NO:1 under stringent hybridization conditions, e.g., hybridization in 0.5 M $NaHPO_4$, 7 percent sodium dodecyl sulfate ("SDS"), 1 mM ethylenediamine tetraacetic acid ("EDTA") at 65° C., and washing in 0.1.times.SSC/0.1 percent SDS at 68°C. (Ausubel et al., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & Sons, Inc. New York, at p. 2.10.3), as well as the proteins encoded by such hybridizing sequences.

Paragraph 46 also states that "[t]he term "MDA-7" as used herein refers to a protein having essentially the amino acid sequence set forth as SEQ ID NO:2, having Genbank Accession Number U16261." The Examiner has not considered the inclusion of "essentially" in this sentence, in the context of the entire paragraph.

The scope of paragraph 46 provides a description of proteins which may be used which is not limited to SEQ ID NO:2, but rather extends to molecules which vary in minor ways and which are functional equivalents to MDA-7. The inclusion of "essentially" conveys that the sequences of proteins encompassed by the claims do not differ in significant ways from SEQ ID NO:2 (they are functionally equivalent) but *CAN* differ in insignificant ways.[1] Accordingly, criteria for similarity that are provided include hybridizability under a set of recited stringent hybridization conditions together with functional equivalence. Applicant asserts that this scope is reasonable and adequately

[1] See the last sentence of paragraph 46 of the published application, which states: "It also includes nucleic acids having essentially the sequence set forth as SEQ ID NO:1, but modified to contain restriction sites appropriate for insertion into a particular expression vector." This shows that *essentially* is used to describe sequences that vary in ways insignificant to the function of the molecule.

described. In fact, the Examiner's contention that the specification does not describe sequence variants ignores express statements to the contrary.

The genus of nucleic acids supported by the specification include molecules which hybridize under the recited conditions and are functionally equivalent to Mda-7. Functions of MDA-7 protein are described in paragraph 15 of the published application in the Background section:

> [0015] When the mda-7 gene was introduced into a wide spectrum of human cancers, growth of cancer cells was inhibited (U.S. Pat. No. 5,710,137 by Fisher, issued Jan. 20, 1998; Jiang et al., 1996, Proc. Natl. Acad. Sci. U.S.A. 93:9160-9165; Su et al., 1998, Proc. Natl. Acad. Sci. U.S.A. 95:14400-14405; Madireddi et al., 2000, Adv. Exptl. Med. Biol. 465:239-261). MDA-7 has been observed to suppress growth in cancer cells which either do not express, or which contain defects in, both retinoblastoma ("rb") and p53 tumor suppressor genes, indicating that mda-7 mediated growth inhibition does not depend on these elements (Jiang et al., 1996, Proc. Natl. Acad. Sci. U.S.A. 93:9160-9165). In contrast to the anti-proliferative effect on various cancer cells, no significant growth inhibitory effect was apparent when this gene was introduced into normal human fibroblast or epithelial cells (Jiang et al., 1996, Proc. Natl. Acad. Sci. U.S.A. 93:9160-9165; Madireddi et al., 2000, Adv. Exptl. Med. Biol. 465:239-261; Saeki et al., 2000, Gene Ther. 7:2051-2057; Mhashilkar et al., 2001, Mol. Med. 7:271-282).

Paragraph 109 of the published specification contains the following sentences:

> Cancer cells susceptible to MDA-7 antiproliferative effects include, but are not limited to, melanoma cells, glioblastoma multiforme cells, osteosarcoma cells, breast cancer cells, cervical cancer cells, colon cancer cells, lung cancer cells, nasopharynx cancer cells, ovarian cancer cells, and prostate cancer cells. A growth suppressive effect of culture medium of Ad.mda-7-infected hepatocytes (providing extracellular MDA-7) on human prostate cancer cells has been observed (see Section 8, below).

Because the specification expressly provides for functional equivalents of MDA-7 bearing minor structural differences relative to the wild-type protein, and because the specification at paragraph 109 of the published application indicates that MDA-7 has an

antiproliferative effect on melanoma cells and paragraph 15 of the published application states that MDA-7 does *not* have a significant antiproliferative effect on normal human fibroblast cells, new claim 82, in addition to requiring that variants hybridize to the entire coding region of the wild type sequence under specified stringent conditions, requires that the encoded proteins inhibit the proliferation of melanoma cells but not normal fibroblast cells. Applicant asserts that new claim 82 meets the requirements of 35 U.S.C. §112 and is otherwise patentable. Accordingly, the rejection for alleged lack of written description should not be applied to new claim 82.

3. **Conclusion**

For the foregoing reasons, it is respectfully requested that claims 81 and 82 be deemed allowable.

Respectfully submitted,

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